

**REMARKS**

Claim 1 has been amended to incorporate therein the features of claims 3-6. Claims 3-6 have been canceled. Further, claim 1 has been amended to recite an average particle size of 10  $\mu\text{m}$  to 1,000  $\mu\text{m}$ , rather than 0.5  $\mu\text{m}$  to 1,000  $\mu\text{m}$ . Support for the lower limit of 10  $\mu\text{m}$  may be found, for example, on the second-to-last line of page 7 of the specification as filed.

No new matter has been introduced. Entry and consideration of the amendments are respectfully requested.

**Response to Claim Rejections - 35 U.S.C. § 103**

A. Claims 1-2, 5-8, and 10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ahn et al. (US 2004/0009614 A1).

Ahn is cited as teaching magnetic bead-based arrays in which magnetic beads are particles that are surface coated with a layer of material suitable for adsorbing or chemically coupling an analyte (par. 37), the beads comprising metallic metal oxides coated with polyethylene or polypropylene (pars. 38-39) and being preferably 1 to 10 microns in size (par. 38).

The Examiner asserts that it would have been obvious to optimize the amount of magnetic material relative to the polymer to meet the features of the present claims for the reason that the amount of magnetic material would directly control the sensitivity of the particles to magnetic radiation/electric field. The ratio of magnetic material to polymer is asserted to be a result effective variable for immunoassays.

Applicants submit that Ahn does not teach or suggest the features of amended claim 1 for at least the following reasons.

First, as recognized by the Examiner, Ahn teaches magnetic beads surface coated with a layer of material suitable for adsorbing or chemically coupling an analyte ([0037]). However, the fine particles of this invention are not coated with a layer of material suitable for absorbing one or more binding molecules. Also, Ahn fails to teach or suggest the claimed functional group recited in amended claim 1.

Second, Ahn teaches away from the claimed particle size. Amended claim 1 recites an average particle size of 10 to 1,000  $\mu\text{m}$ . In contrast, Ahn teaches a preferred average diameter of 1 to 10  $\mu\text{m}$  as described in [0038] of Ahn. In the larger range of particle size, sedimentation controls much of the behavior of the magnetic beads. Therefore the density of the magnetic beads at this range of particle size becomes important, as further described below.

Third, a skilled artisan would not be motivated to optimize the ratio of Ahn as suggested by the Examiner. The Examiner recognizes that Ahn is silent as to the amount of magnetic material relative to the particle (and is thereby silent as to the density of the fine particles).

The claimed fine particles achieve the objects of providing fine particles in which desired magnetic particles are enclosed, the fine particles being easy to handle, having a large surface area, being resistant to settling, being compact, and having a functional group such as a carboxyl group on the particle surface (page 2 of the specification). The particles are evaluated by magnetic responsiveness in the following manner:

“0.1 g of a fine particle sample was dispersed in 5 cc of water in a 10 cc plastic container, and the magnetic responsiveness was defined as good if the magnetic resin particles were drawn toward the container wall within a few seconds when a magnetic field (about 50 kA/m) was applied from the outside of the container using a permanent magnet, and the particles dispersed to the original state without aggregating when the magnet was removed.” (page 11 of the specification)

In response to the Examiner's position that a skilled artisan would recognize the ratio of magnetic material to polymer as a result effective variable, Applicants submit that Ahn neither teaches nor suggests using the particles where magnetic responsiveness is necessary or important. On the contrary, Ahn separates magnetic beads on the substrate through magnetic flux guidances ([0086]) or on a disposable cartridge 70 ([0088]).

Fourth, while Ahn is silent with respect to density, it appears implicit in Ahn that Ahn's magnetic beads would be of much higher density than the claimed density. In describing to the formation of the magnetic beads of Ahn, several references are cited in [0038]. Ahn, and the incorporated references, however, fail to teach the claimed density of Applicants' fine particle. For example, U.S. Pat. No. 5,834,121 to Sucholeiki et al. teaches the use of a vinyl binder for magnetic beads.

Claims 1 and 19 of Sucholeiki are reproduced (with Applicants' emphasis) below:

1. A composite magnetic bead comprising:

- a) microporous matrix of a first polymer, said first polymer comprising at least one vinyl monomer; and
- b) a plurality of primary beads, each primary bead comprising a metal oxide having inducible magnetic properties and a coating of a second polymer that comprises at least one vinyl monomer, said coating encapsulating said metal oxide, wherein said plurality of primary beads is distributed throughout said microporous matrix.

19. A method for making a composite magnetic bead having a plurality of primary beads randomly distributed throughout said composite magnetic bead, said method comprising the steps of

- (1) preparing a continuous fluid phase comprising a solvent and a dispersing agent;
- (2) preparing a dispersed phase comprising:
  - (a) said plurality of primary beads, where each of said primary beads comprises a metal oxide particle having inducible magnetic properties and of a rigid polymeric coating encapsulating said metal oxide particle;
  - (b) at least one vinyl monomer selected from the group consisting of styrenes, methacrylates, acrylates, and derivatives thereof, and

- (c) an inert diluent;
- (3) mixing said dispersed phase with said continuous fluid phase to form an emulsion having a plurality of droplets, each droplet containing said primary beads, each droplet having a diameter greater than 10 microns,
- (4) adsorbing said vinyl monomer onto said rigid polymeric coating of each of said plurality of primary beads; and
- (5) polymerizing said vinyl monomer to provide a microporous polymeric matrix interlinking said primary beads.

As shown above, Sucholeiki uses a vinyl binder for magnetic beads. Since the density of a vinyl polymer itself is generally above 1.1 g/cc, the density of the resulting magnetic beads of Sucholeiki (and of Ahn) is much higher than 1.1 g/cc. Further, in Ahn, the “polymeric coating” is a polymeric coating coated on the magnetic beads. Polyethylene and polypropylene are included as coating polymers ([0039]). A polyolefin is not suitable as a coating material on the magnetic beads since a polyolefin is not soluble in ordinary solvents.

On the other hand, the claimed fine particle uses a polyolefin or a polyolefin copolymer as the sole binder to enclose a magnetic material. Thus, a low density of 1.0-1.1 g/cc has been achieved.

For at least the reasons above, reconsideration and withdrawal of the rejection are respectfully requested.

**B.** Claims 3-4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ahn as applied to claims 1-2, 5-8, and 10, in view of Guo et al. (US 6,177,088).

Ahn is cited as teaching a functionalized coating but fails to teach the functional group of amended claim 1 (canceled claim 3). Guo is cited as teaching surface-functionalized, probe-containing nanospheres surface coated with carboxylic acid groups, which will bind with antigens for immunoassay procedures (ab.; c. 4, II. 35-54; c. 4, I. 64 to c. 5, I. 15). Guo’s

compounds containing the carboxylic acid groups are further cited as containing a terminal olefin, to bind with the outer shell (c. 4, II. 35-54).

The Examiner asserts that it would have been obvious to polymerize Guo's acid-compound into the beads of Ahn to attach antigens for immunoassays.

Claims 3-4 are patentable over Ahn in view of Guo for at least the reasons explained above, for which claim 1 is patentable.

As recognized by the Examiner, Ahn teaches magnetic beads surface coated with a layer of material suitable for adsorbing or chemically coupling an analyte ([0037]). However, the fine particles of the present invention are not coated with a layer of material suitable for absorbing one or more binding molecules. Also, Ahn fails to teach or suggest the claimed functional group recited in amended claim 1. Guo does not cure the deficiency of Ahn in this respect.

Also, a skilled artisan would not have combined Guo and Ahn in the manner suggested. Guo is directed to nanospheres having diameters of less than about 50 nm, whereas the claimed fine particles have an average particle size of 10  $\mu\text{m}$  to 1,000  $\mu\text{m}$ . Guo's nanospheres have probe ion cores surrounded by layers of surfactant and by a polymer shell (Abstract). In contrast, particles of this invention are not surrounded by layers of surfactant.

Guo teaches vinyl copolymer nanospheres in Example 1 including styrene, divinyl benzene, 2,3-dimethyl-1,3-butadiene, etc. (col. 8, lines 49-55). The presently claimed fine particle, however, uses a particle binder of polyolefin or polyolefin copolymer. For these reasons, Applicants dispute the Examiner's position that a skilled artisan would have combined Guo with Ahn.

Reconsideration and withdrawal of the rejection are respectfully requested.

C. Claims 7 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ahn as applied to claims 1-2, 5-8, and 10, in view of Goldman et al. (US 4,097,392).

Ahn is cited as teaching using nickel- or manganese-ferrites (par. 38) but fails to teach using a manganese-zinc ferrite, a nickel-zinc ferrite, or a combination thereof as the magnetic material, as claimed. Goldman is cited as teaching a method for manufacturing soft ferrite materials, including nickel-zinc ferrites and manganese-zinc ferrites (c. 10, II. 66-67).

The Examiner asserts that it would have been obvious to use nickel-zinc ferrites or manganese-zinc ferrites as the magnetic material of Ahn because the presence of zinc would be expected to alter the magnetic characteristics of the composite.

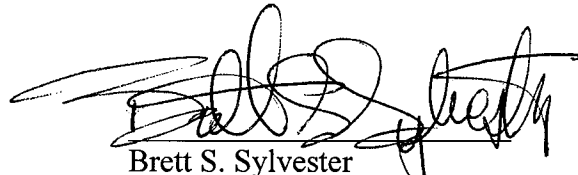
Claims 7 and 9 are patentable over Ahn in view of Goldman for at least the reasons cited above, for which claim 1 is patentable. Further, Goldman discloses a wet process for producing soft ferrite materials but is silent as to whether it is suitable to improve magnetic responsiveness in magnetic particles. Accordingly, Applicants dispute that a skilled artisan would have used a soft magnetic material in magnetic particles of this invention in view of Goldman.

Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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